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L5: Entry 96 of 103 File: USPT May 20, 1997

US-PAT-NO: 5631236
DOCUMENT-IDENTIFIER: US 5631236 A

TITLE: Gene therapy for solid tumors, using a DNA sequence encoding HSV-Tk or VZV-Tk

DATE-ISSUED: May 20, 1997

US-CL-CURRENT: 514/44; 424/93.6, 435/320.1

APPL-NO: 8/ 112745 [PALM]
DATE FILED: August 26, 1993

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Abstract Paragraph Left (1):
The present invention provides a novel method of treating localized solid tumors and papilloma in an individual. The method comprises introducing a recombinant adenoviral vector containing the herpes simplex virus-thymidine kinase gene. Subsequently, a prodrug, such as the drug ganciclovir, is administered to the individual. The methods of the present invention may be used to treat several different types of cancers and papillomas, including colon carcinoma, prostate cancer, breast cancer, lung cancer, melanoma, hepatoma, brain and head and neck cancer.

Drawing Description Paragraph Right (5):
FIG. 5 shows the strategy for gene therapy of brain tumors using recombinant adenoviral vectors containing HSV-TK.

Detailed Description Paragraph Right (6):
Recombinant adenoviruses containing the HSV-TK gene can be driven by various promoters including that of the cytomegalovirus, Rouse sarcoma virus LTR, murine leukemia virus LTR, simian virus 40 early and late, and endogenous HSV-TK genes. The recombinant adenoviruses are used to efficiently deliver the HSV-TK gene to tumors.

Detailed Description Paragraph Right (22):
The strategy for gene therapy of brain cancer using recombinant adenoviral vectors containing HSV-TK is shown in FIGS. 5 and 6. In FIG. 5, C6 glioma cells were injected stereotactically into nude mouse brain with a little charcoal to mark the site of injection. About 1 week later, Ad/RSV-TK was injected into the tumor stereotactically. The mice were then divided into 2 groups, one treated with ganciclovir for 6 days and the other with phosphate-buffered saline (PBS). The animals were then kept without further treatment until tumors developed, i.e., about one to two weeks.

Detailed Description Paragraph Right (24):
Experimental animals were inoculated with 10.sup.4 C6 glioma cells by stereotactic injection into the brain. After 4-8 days, 3.times.10.sup.8 particles of recombinant adenoviral vector containing the HSV-TK (Ad/RSV-TK) gene were stereotactically injected into the same site. Twelve hours later, the animals were either treated i.p. daily with buffer (PBS) or Ganciclovir (GCV:125 mg/kg) for 6 consecutive days. The animals were kept without further treatment until the 20th day from the day of tumor cell inoculation and the appearance of brain tumors for individual animals was recorded.

Detailed Description Paragraph Right (32):
Cell-type specificity of HSV-TK gene expression after recombinant adenoviral vector administration in a particular solid tumor, papilloma or wart can also be achieved with the use of tissue-specific promoters to direct the transcription of the HSV-TK gene. Some examples of the various tissue specific promoters are shown in Table II.

Detailed Description Paragraph Table (1):
TABLE I _____ Brain Tumor Treatment with an Adenoviral Vector having the HSV-TK Gene TREATMENT PBS GCV

Number of Treated Animals 4 4 Number of Animals with Brain Tumor 4 1

CLAIMS:

1. A method of causing regression of a solid tumor in a mammal comprising the steps of,

introducing an adenoviral vector directly into said tumor wherein said vector is comprised of a DNA sequence encoding HSV-tk operatively linked to a promoter and wherein said tumor express HSV-tk; and

administering ganciclovir, acyclovir or FIAU in amounts sufficient to cause regression of said tumor when said ganciclovir, acyclovir or FIAU is converted to a toxic compound by HSV-tk.